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REQUEST FOR CERTIFICATE OF
CORRECTION UNDER 37 CFR 1.322
Docket No. FIT-100XC1
Patent No. 6,847,700


James S. Parker, Patent Attorney

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Kunai Mitra, Charles R. Lambert
Issued : January 25, 2005
Patent No. : 6,847,700
For : Method and Apparatus for Delivery of X-Ray Irradiation

Mail Stop Certificate of Corrections Branch
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REQUEST FOR CERTIFICATE OF CORRECTION
UNDER 37 CFR 1.322 (OFFICE MISTAKE)

Sir:

A Certificate of Correction (in duplicate) for the above-identified patent has been prepared and is attached hereto.

In the left-hand column below is the column and line number where errors occurred in the patent. In the right-hand column is the page and line number in the application where the correct information appears.

Patent Reads:

Column 2, line 23:
"radiation"

Column 4, line 59:
"location X-ray"

Application Reads:

Page 3, line 2:
--Irradiation--

Page 6, line 25:
--location. X-ray--

Column 8, line 51:
“parabolic beat”

Column 13, line 14:
“Belenger, I.,”

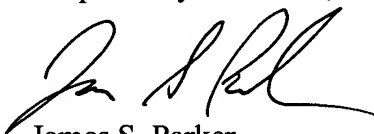
Page 12, line 13:
--parabolic heat--

Page 20, line 28:
--Belenger, J.,--.

A true and correct copy of pages 3, 6, 12, and 20 of the specification as filed which supports Applicants' assertion of the errors on the part of the Patent Office accompanies this Certificate of Correction.

Approval of the Certificate of Correction is respectfully requested.

Respectfully submitted,



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Attachments: Certificate of Correction in duplicate; copy of page 3, 6, 12, and 20 of the specification

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 6,847,700

Page 1

DATED : January 25, 2005

INVENTORS : Mitra *et al.*

It is certified that errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 2,

Lines 23, "radiation" should read --Irradiation--.

Column 4,

Line 59, "location X-ray" should read --location. X-ray--.

Column 8,

Line 59, "parabolic beat" should read --parabolic heat--.

Column 13,

Line 14, "Belenger, I.," should read --Belenger, J.,--.

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PATENT NO. 6,847,700

No. of additional copies





- Sawetprachkul, A., Hsu, P., and Mitra, K., "A Monte Carlo Study of the Transient Radiative Transfer within the One-Dimensional Layered Slab," to be presented at International Mechanical Engineering Congress and Exposition, Orlando (Florida), November 5-10 (2000).

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- ✓ Schatz, R., Baim, D., and Leon, M., "Clinical Experience with the Palmaz-Schatz Coronary Stent," *Circulation*, Vol. 83, pp. 148-161 (1991).

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- ✓ Serruys, P., De Jaegere, P., Kiemeneji, F., Macaya, C., Rutsch, W., Margo, J., Materne, P., Sigwart, U., Colombo, A., Delcan, J., and Morel, M., "A Comparison of Balloon-Expandable-Stent Implantation with Balloon Angioplasty in Patients with Coronary Artery Disease," *The New England Journal of Medicine*, Vol. 331, no. 8, pp. 489-495 (1994).

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- ✗ Siegel, R., and Howell, J.R., *Thermal Radiation Heat Transfer*, 3rd ed., McGraw-Hill, New York (1992).

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- ✓ Teirstein, P.S., Massullo, V., Jani, S., Russo, R., Schatz, R., Sirkin, K., Norman, S., and Tripuraneni, P., "Two-Year Follow-Up after Catheter-Based Radiotherapy to Inhibit Coronary Restenosis," *Circulation*, Vol. 99, no. 2, pp. 243-247 (1999).

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- ✓ Topol, E.J., Leya, F., and Pinkerton, C.A., "A Comparison of Directional Atherectomy with Coronary Angioplasty in Patients with Coronary Artery Disease," *The New England Journal of Medicine*, Vol. 329, pp. 221-227 (1993).

- ✓ Vedavarz, A., Kumar, S., and Moallemi, M.K., "Significance of Non-Fourier Heat Wave in Conduction," *ASME Journal of Heat Transfer*, Vol. 116, pp. 221-224 (1994).

- ✓ Verin, V., Popovski, Y., Urban, P., Belenger, J., Redard, M., Costa, M., Widmer, M., Rouzaud, M., Nouet, P., Grob, E., Schwager, M., Kurtz, J., and Rutishauser, W., "Intra-

where \bar{q} is heat flux, T is the temperature, w is the blood perfusion rate, r_b is the density of blood, C_b is the specific heat of blood, ρ is the density of tissue, C is the specific heat of tissue, κ is the thermal conductivity of tissue, and τ is the thermal relaxation time of tissue. The relaxation time of the tissues can be experimentally obtained (Mitra, K., Kumar, S., Vedavarz, A., and Moallemi, M.K., "Experimental Evidence of Hyperbolic Heat Conduction Waves in Processed Meat," Journal of Heat Transfer, Vol. 117, no. 3, pp. 568-573 (1995)). Equation (3) is the hyperbolic or wave model of heat conduction proposed by Cattaneo, C., "A Form of Heat Conduction Equation Which Eliminates the Paradox of Instantaneous Propagation," Comptes Rendus, Vol. 247, pp. 431-433 (1958) and Vernotte, M.P., "Les Paradoxes de la Theorie Continue de l'Equation de la Chaleur," Comptes Rendus, Vol. 246, pp. 3154-3155 (1958) and accounts for finite speed of propagation of thermal signals. If the second term on the left hand side of Equation (3) is neglected it becomes the Fourier or parabolic heat conduction model and it implies a physically unrealistic infinite propagation speed of the temperature signal.

Equations (2) and (3) can be combined to obtain

$$\nabla^2 T = \left(\frac{1}{\alpha} + \frac{\tau \omega \rho_b C_b}{\kappa} \right) \frac{\partial T}{\partial t} + \frac{\tau}{\alpha} \frac{\partial^2 T}{\partial t^2} + \frac{\omega \rho_b C_b}{\kappa} T - \frac{\sigma_a}{\kappa} I - \frac{\sigma_a}{\kappa} \frac{\partial I}{\partial t} \quad (4)$$

where α is the thermal diffusivity. Equation (4) is a hyperbolic partial-differential equation and yields a finite wave speed ($= \sqrt{\alpha/\tau}$) for the propagation speed of the temperature signals. In the limit $t \rightarrow 0$, Equation (4) becomes the parabolic or Fourier heat conduction equation.

Most previous work for such analysis have used Fourier heat conduction model. A sample result showing the non-dimensional temperature distribution comparison between hyperbolic and Fourier heat conduction equation is presented in Figure 10. The case under consideration is a two-dimensional axis-symmetry geometry (r - z coordinate system). It could

Figure 5 illustrates a comparison of the mechanism of treating a tumor via thermal treatment and treating a tumor via x-ray irradiation in accordance with the subject invention.

Figure 6 illustrates the relationship between the x-ray energy and the HVL.

Figure 7 shows an x-ray generation device in accordance with the subject invention.

Figure 8 illustrates an overall view of an arterial treatment in accordance with the subject invention.

Figure 9 illustrates a conical reflecting tip in accordance with the subject invention..

Figure 10 shows a comparison between hyperbolic and fourier heat conduction equation model.

Detailed Description of the Invention

The subject invention relates to a method and apparatus for the generation and/or delivery of x-rays. In a specific embodiment, the subject invention can utilize hollow waveguides to convey x-ray radiation generated outside of the body into the body to a specific internal surface for a variety of purposes, for example, for medical therapy. For example, the x-ray radiation can be delivered to an arterial wall for the prevention of restenosis following balloon angioplasty. In another embodiment, the x-ray radiation can be delivered into the body to kill tumors with a lesser degree of collateral damage to body tissue than has previously been realized. The x-ray radiation used to treat tumors, for example, can be collected by non-imaging optics and delivered through stereotactically guided needles by hollow waveguides.

X-ray radiation has several applications in the medical field. In addition to imaging, x-rays can be used as a therapy treatment to treat numerous medical conditions. The subject invention can be utilized to control and deliver a precise dose of x-ray radiation to a target location. X-ray radiation can be generated for example, by bombarding a metal target with energetic electrons in a vacuum tube. The energy of the x-ray radiation depends on the voltage applied to the vacuum tube. Hollow waveguides have been used for x-ray transmission by D. Mosher, S.J. Stephanakis, I.M. Vitkevitsky, C.M. Dozier, L.S. Levine and D. J. Nagel, Appl. Phys Lett. 23, pp. 429-431 (1973), D. Mosher and S.J. Stephanakis, "X-ray "light pipes," Appl.Phys. Lett, 29, pp. 105 -107 (1976), and M. A. Kumakhov,

(Waksman, R., Roninson, K.A., Crocker, R., Gravanis, B., Cipolla, G., and King, S., "Endovascular Low Dose Irradiation Inhibits Neointimal Formation After Coronary Artery Balloon Injury in Swine: A Possible Role for Radiation Therapy in Restenosis Prevention," Circulation, Vol. 91, pp. 1533-1539 (1995); Weidemann, J.G., Marboe, C., Almos, H., Schwartz, A., and Weinberger, J., "Intracoronary Irradiation Markedly Reduces Neointimal Proliferation After Balloon Angioplasty in Swine," Journal of American College of Cardiology, Vol. 25, pp. 1451-1456 (1995); Verin, V., Popovski, Y., Urban, P., Belenger, J., Redard, M., Costa, M., Widmer, M., Rouzaud, M., Nouet, P., Grob, E., Schwager, M., Kurtz, J., and Rutishauser, W., "Intra-arterial Beta Irradiation Prevents Neointimal Hyperplasia in a Hypercholesterolemic Rabbit: Restenosis Model," Circulation, vol. 92, pp. 2284-2290 (1995); Teirstein, P.S., Massullo, V., Jani, S., Russo, R., Schatz, R., Sirkin, K., Norman, S., and Tripuraneni, P., "Two-Year Follow-Up after Catheter-Based Radiotherapy to Inhibit Coronary Restenosis," Circulation, Vol. 99, no. 2, pp. 243-247 (1999)). Thus, there is a need for a treatment of restenosis which can reduce the drawbacks associated with current treatments.

There is uncertainty as to the healing mechanism of x-ray irradiated injured vessels. Also, it is not clear what long-term side effects of irradiation therapy there may be. It appears that a safe dosage rate is on the order of 8-30 Gy (1 Gy = 1 J/kg), while lower radiation doses appear to be unable to significantly inhibit restenosis (Coursey, B.M., and Nath, R., "Radionuclide Therapy," Physics Today, pp. 25-30, April (2000).

Summary of the Invention

The subject invention pertains to a method and apparatus for generation and/or delivery of x-ray irradiation. The subject method and apparatus provides for the controlled delivery of x-ray radiation to specific parts of a patient's body. The subject invention can be used in the treatment or prevention of restenosis to aid in the prevention of arterial clogging. Additionally, the subject invention is particularly advantageous in situations requiring precise maneuvering due to the lack of radiation generating sources that are introduced into the body as taught by the prior art. Accordingly, there is a need for a method and apparatus for providing a non-invasive procedure which can deliver a highly controlled dose of x-ray